progesterone—norethindrone and norgestrel—tend to reverse the beneficial changes seen with estrogen alone, whereas medroxyprogesterone acetate has the least, if any, adverse effect on blood lipids.

The preponderance of data would indicate that estrogen replacement therapy after menopause elicits a cardioprotective effect. The effect of adding progestin to estrogen replacement is unknown at this time, but because progestin is necessary to reduce iatrogenic malignancy, it must be added. In choosing a progestin, the lowest dose possible should be used and a product prescribed that has the least undesirable effects on blood lipids. Thus, the most appropriate combination would include medroxyprogesterone acetate added to an orally prescribed estrogen.

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REFERENCES

Bush TL, Barrett-Connor E, Cowan LD, et al: Cardiovascular mortality and noncontraceptive use of estrogen in women: Results from the Lipid Research Clinics Program Follow-up Study. Circulation 1987; 75:1102-1109

Corson SL: Impact of estrogen replacement therapy on cardiovascular risk. J Reprod Med 1989; 34:729-746

Matthews KA, Meilahn E, Kuller LH, et al: Menopause and risk factors for coronary heart disease. N Engl J Med 1989; 321:641-646

Gonadotropin-Releasing Hormone Agonist Treatment of Endometriosis and Myomas

OVER THE PAST decade, several structural analogues of gonadotropin-releasing hormone (GnRH) have been described that simulate its action if administered in a pulsatile fashion (agonists) and counteract its effects if given in a nonpulsatile fashion (antagonists). A down regulation of pituitary GnRH receptors results in an initial release of luteinizing and follicle-stimulating hormone reserve pools in gonadotrophs, followed by a protracted state of decreased gonadotropin secretion and, therefore, decreased ovarian estradiol (E_2) production. Because these agents promote a hypoestrogenic state, their usefulness lies in the treatment of E_2-dependent disorders including uterine leiomyomata and endometriosis.

Several studies have shown that treatment with a GnRH agonist will ameliorate symptoms associated with uterine leiomyomata. The response of individual fibroids to GnRH-agonist therapy varies widely, with a 10% to 80% decrease in size reported after three to six months of treatment, presumably because of different E_2 sensitivities of fibroids—such as more fibrous tumors with decreased E_2 sensitivity. In general, a marked reduction in fibroid size occurs by three months of treatment. An overall decrease in total uterine volume, more predictable than a decrease in myoma size, is also complete by about three months of treatment. As fibroids decrease in size, tissue planes are easier to identify and surgical extirpation is easier. In addition, uterine blood flow is diminished in the hypoestrogenic state induced by the GnRH agonist. Amenorrhea preoperatively allows a patient to replenish her hemoglobin supplies and to bank autologous blood. Also, decreased blood loss at the time of the operation decreases the need for intraoperative or postoperative blood transfusions and the likelihood of postoperative adhesion formation. Gonadotropin-releasing hormone agonists are best used as adjuncts to surgical treatment because once treatment is stopped and ovarian function resumes, usually within six weeks after stopping therapy, fibroids will regrow to their pretreatment size within four months.

Endometriosis implants are exquisitely sensitive to E_2, and GnRH-agonist therapy with ensuing hypoestrogenism is well suited to the treatment of this condition. About 80% of women with endometriosis and pelvic pain will experience notable amelioration of their symptoms within six weeks of therapy. An objective response of pelvic endometriosis to GnRH-agonist therapy has been documented, and conservative surgical therapy is generally easier after several months of treatment because of a decreased vascularity of the lesions and easier tissue planes for dissection. As with fibroids, the effects of the GnRH agonists are at best temporary, and the benefits of treatment must be weighed with the risks associated with hypoestrogenism, including decreased (reversible) bone density and possible alterations in high- and low-density lipoprotein cholesterol.

The only GnRH agonist that has been approved by the Food and Drug Administration is leuprolide acetate (Lupron, TAP Pharmaceuticals, North Chicago), and this approval is for prostate cancer treatment. Leuprolide is available in subcutaneous or intramuscular (depot) form. Doses of 0.5 to 1.0 mg subcutaneously daily for three months for fibroids or for six months for endometriosis are generally recommended. Alternatively, 3.75 mg given intramuscularly every 28 days is recommended for the depot form of the drug. It is advisable to begin administering it between days 1 and 3 of the menstrual cycle to obtain rapid ovarian suppression. Most women will become amenorrheic by four weeks of therapy. The main side effects are hot flashes and headaches. Patients expected to be on GnRH-agonist therapy for a protracted course would benefit from bone densitometry studies. Monthly checks of cholesterol levels may be useful.

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REFERENCES

Friedman AJ, Barbieri RL: Leuprolide acetate: Applications in gynecology. Curr Probl Obstet Gynecol Fertil 1988; 11:205-236

March CM: Update: Uses of GnRH agonists in gynecologic practice. Endocr Fertil Forum 1989; 12:1-6

Endometrial Ablation

ENDOMETRIAL ABLATION using the neodymium:YAG [yttrium-aluminum-garnet] laser resectoscope with roller-ball or wire-loop electrocautery is an effective alternative to hysterectomy for women with excessive uterine bleeding refractory to surgical or medical therapy. It is an outpatient procedure done under general or occasionally regional anesthesia with minimal inconvenience, cost, and almost no discomfort to the patient. With recent approval by the Food and Drug Administration, this procedure is no longer considered experimental. It is for women whose uterus is otherwise normal or contains small fibroids, who have unusually heavy or prolonged bleeding or excessive intermenstrual bleeding. Before the procedure is done, they should have had a hysteroscopy with endometrial biopsy or dilatation and curettage to rule out endometrial carcinoma, endometrial atypia, endometrial polyp, or submucosal myoma. The first two are contraindications to endometrial ablation, and the latter two can usually be treated specifically without the need for ablation. An adequate trial of hormonal management to control bleeding is recommended before ablation.

The basic principle of endometrial ablation is to destroy the endometrium, hence controlling excessive menstrual flow. The procedure is done by inserting a hysteroscope into the uterine cavity, distending it with a clear fluid medium to